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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,387	10/25/2005	Yoseph Shaaltiel	30570	1887

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MARTIN D. MOYNIHAN d/b/a PRTSI, INC.
P.O. BOX 16446
ARLINGTON, VA 22215

EXAMINER	
RAMIREZ, DELIA M	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
04/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,387	SHAALTIEL ET AL.	
	Examiner	Art Unit	
	DELIA M. RAMIREZ	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73-98,100,103,106-109,114,115,117,120,121 and 124-149* is/are pending in the application.

4a) Of the above claim(s) *73-97,103,121 and 129-141* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *98,100,106-109,114,115,117,120,124-128 and 142-149* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 December 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/8/08;12/28/08;2/1/08*.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application

6)☒ Other: *alignment*.

DETAILED ACTION

Status of the Application

Claims 73-98, 100, 103, 106-109, 114-115, 117, 120-121, 124-149 are pending.

Applicant's amendment of claims 98, 106-109, 114-115, 120, 124-127, 142-143, addition of claims 145-149, cancellation of claims 99, 101-102, 104-105, 110-113, 116, 118-119, 122-123, amendments to the specification and the drawings, as submitted in a communication filed on 12/22/2008 are acknowledged.

Applicant's submission of a new sequence listing in a communication filed on 2/17/2009 is acknowledged.

New claims 145-149 are deemed directed to the elected subject matter. As previously indicated, claims 73-97, 103, 121, 129-141 remain withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Linking claim 98 is not deemed allowable at this time, thus the restriction requirement can be properly maintained. Claims 98, 100, 106-109, 114-115, 117, 120, 124-128, 142-149 are at issue and are being examined herein.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Information Disclosure Statement

1. The information disclosure statements (IDS) submitted on 8/8/2008, 12/28/2008, 2/1/2008 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Specification

2. The previous objection to the title of the invention as being not descriptive and the objection to the specification for not complying with sequence rules are hereby withdrawn by virtue of applicant's amendment.

3. The amendment filed 2/17/2009 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material is not supported by the original disclosure for the following reasons. A new sequence listing where the previous SEQ ID NO: 8 has been replaced with a new SEQ ID NO: 8 is acknowledged. Applicant has indicated that due to an unintentional mistake the incorrect sequence was used as SEQ ID NO: 8. Applicant has referred to specific portions of the specification to indicate that there is support for the new SEQ ID NO: 8. Specifically, Applicant refers to portions of the specification which state that (1) the polynucleotide of SEQ ID NO: 7 encodes the polypeptide of SEQ ID NO: 8, (2) the polypeptide of SEQ ID NO: 14 comprises SEQ ID NO: 8, (3) a reference to an ATCC deposit which comprises a nucleic acid encoding the polypeptide of SEQ ID NO: 8, and (4) the functional/structural characteristics described for the polypeptide of SEQ ID NO: 8 which can only be those of a protein comprising the new SEQ ID NO: 8. Upon aligning SEQ ID NO: 14 as originally filed and the new SEQ ID NO: 8, it has been found that SEQ ID NO: 14 does not comprise the new SEQ ID NO: 8. Furthermore, an alignment of SEQ ID NO: 7 as originally filed against SEQ ID NO: 14 shows a perfect alignment, thus indicating that SEQ ID NO: 7 cannot encode the new SEQ ID NO: 8. See attached alignment. There is a gap around amino acid 287 of the new SEQ ID NO: 8. Since the new SEQ ID NO: 8 does not appear to be comprised by SEQ ID NO: 14 as originally filed, or encoded by SEQ ID NO: 7 as originally filed, the new sequence listing introduces new matter into the disclosure. Applicant is required to cancel the new matter in the reply to this Office Action.

Drawings-Petition

4. A petition filed on 12/22/2008 under 37 CFR 1.84(a)(2) to accept color photographs and/or color drawings is hereby granted. As required by 37 CFR 1.84, the petition is accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, and an amendment to include the required paragraph in the brief description of the drawings section. Thus, the conditions for accepting color drawings/photographs have been satisfied.

Claim Rejections - 35 USC § 112, Second Paragraph

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 127 remains rejected and claims 109, 120, 148 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment

7. Claims 109, 120 are indefinite in their recitation of "protein/preparation of claim 98/115 wherein said ….. comprises the amino acid sequence as set forth in SEQ ID NO: 8" because the protein recited in claims 98/115 cannot comprise SEQ ID NO: 8 as currently presented. See extensive discussion above regarding why SEQ ID NO: 7 does not encode SEQ ID NO: 8 as amended. Therefore, claims 109, 120 are of different scope and do not further limit claims 98/115. Correction is required.

8. Claim 127 is indefinite due to the recitation of "cell preparation ….protein having at least one xylose residue and at least one exposed mannose residue is the main glycan structure of the lysosomal proteins of said plant cell preparation". As written, it appears as if (1) the protein is a glycan structure, and (2) the cell preparation comprises other lysosomal proteins. As known in the art, a protein is not a glycan structure. Moreover, it is unclear as to which are the other lysosomal proteins being referred to. If the claim is simply attempting to indicate that the main glycan structure found in the human lysosomal

protein of that cell preparation comprises a xylose residue and at least one exposed mannose residue, it is suggested that the claim be amended accordingly. For examination purposes, claim 127 will be assumed to be a duplicate of claim 115. Correction is required.

9. Claim 148 is indefinite in the recitation of "protein of claim 147 having uptake into macrophages" as it is unclear how a protein can have uptake. If the intended limitation is that the protein can be taken by macrophages, the claim should be amended accordingly. For examination purposes, claim 148 will be considered a duplicate of claim 147. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 98-102, 104-108, 110-119, 122-128 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description and enablement requirements. In view of the fact that the claims are now limited to a protein which comprises SEQ ID NO: 8 and compositions thereof, these rejections are hereby withdrawn.

12. Claims 109, 120, 142, 144 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection necessitated by amendment.

The instant claims are now directed to a protein, or composition thereof, wherein said protein which comprises an amino acid sequence for which the Examiner has not been able to find support (new SEQ ID NO: 8). See the new matter objection made to the specification for extensive discussion as to

why there is no support for the new SEQ ID NO: 8. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 102

13. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

14. Claims 98-102, 110-119, 127, 128 were rejected under 35 U.S.C. 102(b) as being anticipated by Garger et al. (U.S. Publication 2002/0088224, published 7/4/2001; application No. 09/993059 filed on 11/13/2001).

15. While Garger et al. teach the recombinant production of human glucocerebrosidase in transgenic tobacco plants wherein said glucocerebrosidase has the recited glycosylation pattern, Garger et al. do not teach a glucocerebrosidase which comprises the new SEQ ID NO: 8, or a glucocerebrosidase encoded by the polynucleotide of SEQ ID NO: 7, wherein said glucocerebrosidase is contiguously linked at its C terminus to a vacuolar targeting signal peptide and at its N terminus to an endoplasmic reticulum signal peptide. Therefore, the previous rejection of the instant claims is hereby withdrawn.

Claim Rejections - 35 USC § 103

16. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

17. Claims 106-107, 124-125 remain rejected and claims 98, 100, 114-115, 117,127, 128, 146-149 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garger et al. (U.S. Publication 2002/0088224, published 7/4/2001; application No. 09/993059 filed on 11/13/2001) in view of Boller et al. (U.S. Patent No. 6054637, issued 4/25/2000) and further in view of Stomp et al. (U.S. Patent No. 6815184, application 09/915873 filed on 7/26/2001).

18. This rejection as it relates to claims 98, 100, 114-115, 117,127, 128 and new claims 146-149 is necessitated by amendment. The rejection of claims 106-107 124-125 is maintained and further applied to claims 98, 100, 114-115, 117,127, 128, 146-149 for the reasons of record and those set forth below.

19. Applicant argues that (1) Garger et al. teach the secretion of the recombinant human glucocerebrosidase by tobacco leaf cells by direction of the recombinant polypeptide to the endoplasmic reticulum (ER) using an N-terminal ER signal peptide, thus teaching away from vacuolar targeting of the recombinant human glucocerebrosidase, (2) Boller et al. teach methods for expressing plant proteins naturally occurring in the vacuole which lack their vacuolar targeting signal peptides, citing sections of the reference of Boller et al. that teach secretion into the intercellular space by deleting the vacuolar targeting signal, and (3) Stomp et al. teach transformation of duckweed plants with polynucleotides modified for secretion of their protein products by addition of an ER targeting signal, citing sections of the reference of Stomp et al. which refer to signal peptides as directing secretion of the polypeptide into the culture medium. Therefore, Applicant concludes that these references' teachings are counterintuitive to the use of C-terminal signal sequences for vacuolar targeting of recombinant proteins expressed in plant cells.

20. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection or avoid the rejection of claims 98, 100, 114-115, 117,127, 128, 146-149. These claims are directed to a polypeptide which is encoded by the polynucleotide of SEQ ID NO: 7 and is contiguously linked at its C-terminus to the vacuolar targeting signal peptide of SEQ ID NO: 2 and at its N-terminus to an N-terminal endoplasmic reticulum signal peptide. The human glucocerebrosidase of Garger et al. is that disclosed in GenBank accession number GLCM_HUMAN GI 121283 (first available on April 23, 1993). The polynucleotide of SEQ ID NO: 7 encodes that polypeptide. The vacuolar targeting signal peptide of SEQ ID NO: 2 is taught by Boller et al. The Examiner acknowledges the sections of the references cited by Applicant but disagrees with Applicant's contention that these

references teach away from using a C-terminal vacuolar signal peptide. As known in the art and admitted by Applicant in the specification (page 7, lines 6-7), an ER signal peptide will direct a protein to the endoplasmic reticulum. Once it is in the ER, the protein will continue to be transported to its final destination (e.g., vacuoles, intercellular environment). Therefore, the teachings of Stomp et al. are not counterintuitive as suggested by Applicant because the addition of the ER signal peptide to the protein of Stomp et al. simply placed the protein in the ER so that from there it was transported to its final destination, which in that case was the intercellular environment (i.e., secretion to the culture medium). The teachings of Stomp et al. and the knowledge of the art would have indicated to one of ordinary skill in the art that because the ER signal peptide was linked to the N-terminus of the desired protein, the protein was transported to the ER, which is what allowed the protein to be eventually secreted to the culture medium. Without transport to the ER, secretion would have been unlikely.

With regard to the teachings of Boller et al., while it is agreed that Boller et al. teach deleting or inactivating the C-terminus vacuolar signal peptide to allow a protein which is naturally retained in the vacuole to be secreted to the medium, Boller et al. also teach that (1) one of the advantages in directing proteins to the vacuole is the fact that vacuoles constitute the largest storage compartment in plants for dissolved substances (column 2, line 57-column 3, line 1), and (2) one could add the DNA encoding the vacuolar signal peptide to the 3' end of any desirable expressible DNA (C-terminus of the corresponding protein). Thus, simply because Boller et al. also teach situations when deleting the vacuolar signal peptide may be advantageous, is not sufficient for one of skill in the art to reasonably conclude that Boller et al. teach away from using a vacuolar signal peptide, particularly in view of the fact that Boller et al. teach advantages in directing proteins to the vacuole. With regard to the teachings of Garger et al., it is noted that while it is agreed that Garger et al. teach that the protein was secreted via a default pathway into the apoplastic compartment, intercellular fluid, cell wall matrix materials, nothing in the teachings of Garger et al., or the prior art, indicates that directing the human glucocerebrosidase to the vacuole would

have a negative effect on the protein. Simply because Garger et al. do not teach redirecting the protein of interest to the vacuole is not sufficient for one of skill in the art to reasonably conclude that Garger et al. teach away from redirecting the protein of interest to the vacuole. Thus, contrary to Applicant's assertions, neither the teachings of Garger et al., Boller et al. or Stomp et al. teach away from directing the human glucocerebrosidase to the vacuole. Therefore, for the reasons of record and those set forth above, one of skill in the art would have to conclude that the claimed invention is obvious over the prior art of record.

21. It is noted that claims 109, 120 have not been rejected in view of the fact that the polypeptide of SEQ ID NO: 8 as currently presented is not taught or suggested in the prior art (deletion around position 287 of SEQ ID NO: 8 with respect to the protein of GenBank GLCM_HUMAN GI 121283).

Double Patenting

22. Claims 98-102, 104-113, 115-120, 122-128 were provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 27-30, 32, 34-39, 41-44, 46-49, 51-52, 55-61 of copending Application No. 11/790991. In view of Applicant's amendments to the claims, particularly claims 98 and 115, this rejection is hereby withdrawn.

23. Claims 114, 142-144 remain provisionally rejected and claims 98, 100, 106-109, 117, 120, 124-128, 145-149 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 39, 45 of copending Application No. 11/790991.

24. This rejection as it relates to claims 114, 142-144 has been discussed at length in previous Office actions. The rejection of claims 114, 142-144 is maintained and further applied to 98, 100, 106-109, 115, 117, 120, 124-128, 145-149 for the reasons of record and those set forth below. This rejection as it relates to claims 98, 100, 106-109, 117, 120, 124-128, 145-149 is necessitated by amendment.

25. Claims 98, 100, 106-109, 114-115, 117, 120, 124-128, 142-149 are directed to (1) a protein which comprises SEQ ID NO: 14, (2) a protein which is encoded by the polynucleotide of SEQ ID NO: 7 and wherein said protein is contiguously linked at the N-terminus to the endoplasmic reticulum signal peptide of SEQ ID NO: 1 and contiguously linked at the C-terminus to the vacuolar targeting signal peptide of SEQ ID NO: 2, and (3) a plant cell preparation comprising (1) or (2), wherein the protein of (1)-(3) contains a xylose residue, exposed mannose residues and a fucose residue having an alpha (1-3) glycosidic bond. Claims 39 and 45 of copending application No. 11/790991 are directed to a human lysosomal protein comprising SEQ ID NO: 8 comprising one xylose residue and one exposed mannose residue, and a pharmaceutical composition comprising said human lysosomal protein. The specification of copending application No. 11/790991 teaches as a preferred embodiment of the invention, the polypeptide of SEQ ID NO: 14, which is the protein of SEQ ID NO: 8 further comprising the signal peptide of SEQ ID NO: 1 at the N-terminus of SEQ ID NO: 8 and the vacuolar targeting signal peptide of SEQ ID NO: 2 at the C-terminus of SEQ ID NO: 8. The specification also discloses as a preferred embodiment of the invention, the plant-glycosylated protein of SEQ ID NO: 14, wherein said protein comprises exposed mannose residues, a xylose residue and a fucose residue. Therefore, in view of the preferred embodiments disclosed in the specification of copending Application No. 11/790991, the invention of claims 98, 100, 106-109, 114-115, 117, 120, 124-128, 142-149 are deemed an obvious variation of the invention of claims 39, 45 of copending Application No. 11/790991.

26. Applicant has indicated that the submission of a terminal disclaimer will be further considered upon indication by the Examiner of allowable subject matter. Since Applicant has not filed a terminal disclaimer or traverse the Examiner's position, this rejection is maintained for the reasons of record.

Conclusion

27. No claim is in condition for allowance.

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

29. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (571) 273-8300. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

30. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez, Ph.D., whose telephone number is (571) 272-0938. The examiner can

normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashaat Nashed can be reached on (571) 272-0934. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

/Nashaat T. Nashed/
Supervisory Patent Examiner, Art Unit 1652

/Delia M. Ramirez/

Primary Patent Examiner
Art Unit 1652

DR
April 8, 2009